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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,683	08/18/2003	James Robert Swartz	STAN-273	4598

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EXAMINER	
VOGEL, NANCY S	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 06/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,683	SWARTZ ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,13,22-25,27 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,13,22-25 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-7 , 13, 22-25, and 27-29 are pending in the case.

Receipt of the Information Disclosure statement on 4/21/06 is acknowledged.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are no new grounds of rejection that were not necessitated by applicants' amendment and therefore, this action is final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-7, 13-25, 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained essentially for the reasons made of record in the previous Office action, mailed 10/20/05, slightly modified for account for the amendments to the claims.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in

the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claims 1 and 13 are drawn to a method of synthesis of polynucleotides or polypeptides in vitro comprising synthesizing said polynucleotides or polypeptides in a reaction mix comprising an extract from bacterial cells, wherein oxidative phosphorylation is activated, magnesium and spermine or spermidine are present, and polyethylene glycol is absent. The term "polynucleotides" includes DNA and RNA.. Applicants have not provided a definition of the phrase "a reaction mix where oxidative phosphorylation is activated", but have described such a reaction mix as being one in which no secondary energy source is needed (page 6). Claims 1 and 13 are genus claims in terms of a method of synthesizing any polypeptide or polynucleotide, including DNA, in vitro, using a reaction mix comprising bacterial extract, wherein oxidative phosphorylation is activated by any means.

The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods of synthesizing any biological macromolecules, or using any reaction mix where oxidative phosphorylation is activated. While the specification provides general information on producing mRNA and polypeptides in an in vitro cell-free expression system, there is no disclosure of the components or conditions necessary for the production of any other type of polynucleotides, such as DNA. Furthermore, while the specification describes the reaction mix prepared from E. coli grown under specific conditions, which result in activated oxidative phosphorylation, there is no disclosure of any other types of reaction mixes having this property, or

guidance regarding the identity of such reaction mixes. Therefore, the specification does not describe the claimed method of synthesis of polynucleotides and polypeptides, using reaction mixes where oxidative phosphorylation is activated, in such full, clear, concise and exact terms so as to indicate that Applicant has possession of the method at the time of filing the present application. Thus, the written description requirement has not been satisfied.

Applicant's arguments filed 4/3/06 have been considered but have not been found convincing.

Applicants have argued that the amendment to the claims, which adds that the reaction mix is substantially free of polyethylene glycol, and a bacterial extract from bacterial cells, with magnesium at 5mM to about 20mM, provides sufficient guidelines for one of skill in the art to practice the claimed methods. However, it is maintained that applicants have not provided a description of any type of bacterial extract based in vitro synthesis method, than that exemplified in the specification. The claims remain genus claims in terms of the recitations of a method of synthesis of polynucleotides in vitro, using bacterial extracts, wherein oxidative phosphorylation is activated, which have not been described in such full, clear, concise and exact terms to indicate Applicant had possession of the method at the time of filing. *Vas-Cath V. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in

the art to recognize that [he or she] invented what is now claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of methods of synthesis in vitro of any polynucleotide or polypeptide using bacterial extracts in which oxidative phosphorylation is activated and no exogenous high energy phosphate source is present, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Col. Ltd.,* 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 recites the limitation "wherein said synthesis further comprises transcription of mRNA from a DNA template", and is dependent on claim 13. However, claim 13 recites a "method for synthesis of polypeptides or polynucleotides in vitro",

which includes transcription of mRNA from a DNA template, and therefore the claim fails to further limit the claim on which it depends.

Claim 25 recites the limitation "said E. coli" in line 1. There is insufficient antecedent basis for this limitation in the claim on which this claim depends, i.e. claim 13.

Claim 27 recites the method of claim 13, wherein the synthesis does not require the addition of a secondary energy source. However, claim 13 recites that the method does not require a secondary energy source ("the absence of an exogenous high energy phosphate source") and therefore the claim fails to further limit the claim on which it depends.

Claim 28 recites the method of claim 13, wherein the synthesis is performed in the absence of an exogenous high energy phosphate source. However, claim 13 recites "the absence of an exogenous high energy phosphate source", and therefore the claim fails to further limit the claim on which it depends.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is advised that should claim 22 be found allowable, claim 29 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 103

Claims 1, 3-7, 13, 22-25, 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable Baranov et al. (Methods in Enzymology, 217, 123-142, 1993) and Chen et al. (Methods in Enzymology, 101, 674-690) (cited for evidentiary purposes only) in view of Yoshida et al. (J. Biol Chem. 274(32), 22723-22728, 1999), Dorner et al. (Proc. Natl. Acad. Sci. USA 76(10):4832-4836, 1979), Shimizu et al. (Nature Biotechnology, 2001, 19 :751-755) (cited by applicants) or Raney et al. (J. Biol. Chem. 275 (32):24444-24450, 2000).

Baranov et al. disclose a method of in vitro synthesis of polypeptides in a reaction mix comprising a biological extract from E. coli grown in glucose containing medium, magnesium at a concentration of from about 5 mM to 20 mM, and substantially free of polyethylene glycol. The reaction mix includes spermidine. See Experiment 5 in Table 1. Note that the E. coli extract is disclosed by Baranov et al. (see page 127, first complete paragraph) as being prepared using a standard method such as that disclosed in Chen et al., Methods in Enzymology, 101, 674-690, in which it is

disclosed that the E. coli is grown in medium containing glucose and phosphate (see page 675, lines 7-11). Baranov et al. discloses continuous flow cell free reactions, in which plasmid is added, and transcription (production of mRNA) and translation of the encoded protein result.

The difference between the reference and the instant claims is that batch process is used and spermine or spermidine is present at about1 mM,.

However, Baranov et al. disclose that the batch process of cell-free transcription and/or translation is known in the art. While the reference does not explicitly disclose the use of the batch process for the experiment disclosed in Table 1, experiment 5, the reference discloses that such a method is well known in the art and is an alternate technique to method of using continuous flow cell free transcription and/or translation. IT would have been obvious to one of ordinary skill in the art to have utilized a batch process of cell free transcription and translation, using the conditions disclosed by Baranov et al., since Baranov et al. disclose that such method was well known and standard practice in the art. One would have been motivated to do so by the well known benefits of ease of practice and simplicity.

In addition, each of Yoshida et al., Dorner et al. Shimizu et al. and Raney et al. disclose in vitro translation systems in which the spermidine is present at a concentration of about 1 mM (see Fig. 4 of Raney et al.; see Table 1 of Dorner et al.; see Figs. 2, 3, 4, of Yoshida et al.; see page 754, second column of Shimizu et al.).

It would have been obvious to one of ordinary skill in the art to have modified the method of in vitro synthesis of polypeptides in a reaction mix by altering the

concentration of spermidine or spermine, including increasing the concentration to about 1 mM, since each of the references Yoshida, Dorner, Shimizu and Raney disclose in vitro translation systems in which varying and increased amounts of spermine and spermidine are present. One would have been motivated to do so by the known effect of spermine and spermidine in in vitro translation, and the known experimental optimization of conditions as disclosed by the references. The references show the state of the art, in which the alteration of the concentration of spermine and spermidine in in vitro translation systems is routine and would have been obvious to one of ordinary skill in the art. Therefore, the invention as currently claimed would have been obvious.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NV
6/22/06

NANCY VOGEL
PRIMARY EXAMINER